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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,721	04/18/2001	Henry Daniell	1463- PCT-US-00	4041
35811	7590	08/12/2005	EXAMINER	
IP GROUP OF DLA PIPER RUDNICK GRAY CARY US LLP			KUBELIK, ANNE R	
1650 MARKET ST			ART UNIT	
SUITE 4900			PAPER NUMBER	
PHILADELPHIA, PA 19103			1638	

DATE MAILED: 08/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/807,721

Applicant(s)

DANIELL ET AL.

Examiner

Anne R. Kubelik

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 June 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,28 and 29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,28 and 29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-2 and 28-29 are pending.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. The rejection of claims 28-29 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention is withdrawn in light of Applicant's amendment of the claim.

Claim Rejections - 35 USC § 112

4. Claims 28-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a plastid transformation vector that transforms tobacco, does not reasonably provide enablement for a plastid transformation vector that transforms any plant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is repeated for the reasons of record as set forth in the Office action mailed 28 January 2005. Applicant's arguments filed 2 June 2005 have been fully considered but they are not persuasive.

The claims are broadly drawn to methods of using plastid transformation vectors comprising plastid DNA, a plastid promoter, a selectable marker sequence, a DNA encoding a humanized Guy's 13 antibody, and transcription termination region, and additional plastid DNA sequence to transform plastids or any plant.

The instant specification, however, only provides guidance for construction of an tobacco plastid expression vector comprising an expression cassette comprising the Guy's 13 heavy chain variable region fused to the mouse IgA2m(2) constant region followed by the Guy's 13 light chain variable region fused to the human kappa constant region (example 1A); transformation of the vector into *E. coli* and analysis of its expression (example 1B); transformation of the vector into tobacco and analysis of the expression of the RNA and protein (examples 1C-F). The specification provides general guidance for Elisa Assay for testing the effectiveness of the antibody produced in the plastids (examples (G-H), and optimization of codon usage (example 2). The specification provides prophetic expression of a construct encoding an IgA heavy chain, a light chain, a J chain and a secretory component or encoding ICAM-1 in tobacco plastids (examples 3-5).

The instant specification fails to provide guidance for methods of using plastid transformation vectors comprising plastid DNA, a plastid promoter, a selectable marker sequence, a DNA encoding a humanized Guy's 13 antibody, and transcription termination region, and additional plastid DNA sequence to transform plastids or any plant, wherein the vectors have flanking sequences that allow the vector to be targeted to the genome of any higher plant chloroplast.

The region of the tobacco plastid genome commonly used for targeting of transformation vectors is not present in the same configuration or sequence in the genomes of other plastids. For example, rice lacks the orf131/orf70B gene (Kanno et al, 1993, Curr. Genet. 23:166-174; see Figure 3). The specification fails to teach a region of the plastid genome that is homologous across all higher plants.

The instant specification also fails to teach transformation of the plastids of any plant species other than tobacco. Heifetz (2000, Biochimie 82:655-666) teaches that reliable and efficient plastid transformation and regeneration of fertile plants with transformed plastids has been limited to tobacco and potato (pg 658, right column, paragraph 2).

As the specification does not describe the transformation of any plant with a plastid transformation vector comprising plastid DNA, a plastid promoter, a selectable marker sequence, a DNA encoding a humanized Guy's 13 antibody, and DNA encoding an chaperonin, and transcription termination region, and additional plastid DNA sequence, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants or algae transformed therewith, to identify those with that express humanized Guy's 13 antibody in their plastids, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, and lack of guidance in the specification as discussed above, the instant invention is not enabled.

Applicant urges that the Guy's 13 gene was inserted into both pZS, a tobacco specific vector, and pLD, a universal vector and successfully transformed into tobacco; pLD has flanking regions that can be used to transform any plant species in the specification (response pg 4).

This is not found persuasive because the only plant species recited in the specification for plastid transformation is tobacco. Thus, the invention remains limited only to tobacco.

Claim Rejections - 35 USC § 103

5. Claims 1-2 and 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over McBride et al in view of Mayfield et al as applied to claims 1-4, 6, 28-31 and 33 above, and

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further in view of Christou et al (US 2002/0078472, filed June 1998). The rejection is repeated for the reasons of record as set forth in the Office action mailed 28 January 2005. Applicant's arguments filed 2 June 2005 have been fully considered but they are not persuasive.

The claims are drawn to plastid transformation vectors encoding a humanized Guy's 13 antibody.

McBride et al disclose a plastid transformation vector comprising an expression cassette comprising a plastid promoter, a DNA sequence encoding a eukaryotic peptide, a termination signal, a second promoter, a selectable marker sequence and a second terminator, wherein the expression cassette is flanked by plastid sequences from a higher plant species (Figure 9) and methods of plastid transformation with the vector (column 17, line 22, to column 18, line 31; column 25, line 18, to column 28, line 14). McBride et al do not disclose vectors encoding a humanized Guy's 13 antibody or with the components in the exact order as claimed in the instant claim 1 and 28.

Mayfield et al teach vectors for transforming the plastids of the algae *Chlamydomonas*, wherein the vectors encodes a tetanus toxin single chain antibody and a dimeric IgA comprising heavy, light and J chains, and wherein the immunoglobulins are part of a polycistronic message (pg 76, line 22, to pg 80, line 31).

Christou et al teach expression of a humanized Guy's 13 antibody, among others (¶102-¶106 and ¶166-¶168).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of plastid transformation as taught by McBride et al, to express DNAs encoding immunoglobulins as described in Mayfield et al. One of ordinary skill in the art

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would have been motivated to do so because of the suggestion of Mayfield et al to produce these proteins in plants (pg 76, line 29) and because of the advantages that expression in plastids provides (McBride et al, column 1, lines 65-67). Expression of the selectable marker and the immunoglobulin on the same construct is suggested by Mayfield et al, who tout the advantages chloroplasts provide for this (pg 78, line 21, to pg 79, line 16). The exact order of the components of the vectors is an obvious design choice. The light chain of the single chain antibody would be an "operative ligand". It would also have been obvious to one of ordinary skill in the art to modify that method of producing immunoglobulins in the plastids, to express a humanized Guy's 13 antibody as described in Christou et al. One of ordinary skill in the art would have been motivated to do so because Christou et al suggests targeting the immunoglobulin to the chloroplast (§20) and because Christou et al touts the advantages of expressing the humanized Guy's 13 antibody in plants (§4).

Applicant urges that the amendment of the claims was intended to address the rejection (response pg 4).

This is not found persuasive because plastid transformation vectors encoding a humanized Guy's 13 antibody are taught in the prior art, as discussed above.

Applicant urges that Christou et al teaches away from the instant invention because it teaches that a chloroplast targeting leader sequence was required and because it teaches nuclear transformation, while the instant claims are directed to plastid transformation (response pg 5).

This is not found persuasive because McBride et al in view of Mayfield et al teach expression of antibodies in plastids. Christou et al teaches a specific antibody whose substitution

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for the antibody taught in McBride et al in view of Mayfield et al would be an obvious design choice.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

6. **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached at (571) 272-0745.

The central fax number for official correspondence is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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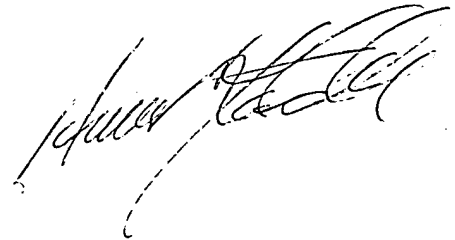
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Anne R. Kubelik, Ph.D.

August 5, 2005

A handwritten signature in black ink, appearing to read 'Anne R. Kubelik', with a long, sweeping horizontal stroke extending to the left.

**ANNE KUBELIK, PH.D.
PRIMARY EXAMINER**